



Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

Downloaded from <https://aidsinfo.nih.gov/guidelines> on 8/31/2020

Visit the AIDSinfo website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at <https://aidsinfo.nih.gov/e-news>.

Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 4)

Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
NNRTIs					
DOR	PK Data	↔ DOR and BIC expected	↔ DOR DTG AUC ↑ 36% and C _{min} ↑ 27%	↑ DOR expected ↔ EVG	↔ DOR and RAL expected
	Dose	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.
EFV	PK Data	↓ BIC expected	With DTG 50 mg Once Daily: • DTG AUC ↓ 57% and C _{min} ↓ 75%	↑ or ↓ EVG, COBI, and EFV possible	With RAL 400 mg Twice Daily: • RAL AUC ↓ 36% and C _{min} ↓ 21% With RAL 1,200 mg Once Daily: • ↔ RAL AUC and C _{min}
	Dose	Do not coadminister.	In Patients Without INSTI Resistance: • DTG 50 mg twice daily In Patients With Certain INSTI-Associated Resistance^a or Clinically Suspected INSTI Resistance: • Consider alternative combination.	Do not coadminister.	No dose adjustment needed.
ETR	PK Data	↓ BIC expected	ETR 200 mg Twice Daily plus DTG 50 mg Once Daily: • DTG AUC ↓ 71% and C _{min} ↓ 88% ETR 200 mg Twice Daily with (DRV 600 mg plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily: • DTG AUC ↓ 25% and C _{min} ↓ 37% ETR 200 mg Twice Daily with (LPV 400 mg plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily: • DTG AUC ↑ 11% and C _{min} ↑ 28%	↑ or ↓ EVG, COBI, and ETR possible	ETR 200 mg Twice Daily plus RAL 400 mg Twice Daily: • ETR C _{min} ↑ 17% • RAL C _{min} ↓ 34%

Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 4)

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
NNRTIs, continued					
ETR	Dose	Do not coadminister.	<p>Do not coadminister ETR and DTG without concurrently administering ATV/r, DRV/r, or LPV/r.</p> <p>In Patients Without INSTI Resistance:</p> <ul style="list-style-type: none"> DTG 50 mg once daily with ETR (concurrently with ATV/r, DRV/r, or LPV/r) <p>In Patients With Certain INSTI-Associated Resistance^a or Clinically Suspected INSTI Resistance:</p> <ul style="list-style-type: none"> DTG 50 mg twice daily with ETR (concurrently with ATV/r, DRV/r, or LPV/r) 	Do not coadminister.	<p>RAL 400 mg twice daily</p> <p>Coadministration with RAL 1,200 mg once daily is not recommended.</p>
NVP	PK Data	↓ BIC expected	<p>With DTG 50 mg Once Daily:</p> <ul style="list-style-type: none"> DTG AUC ↓ 19% and C_{min} ↓ 34% 	↑ or ↓ EVG, COBI, and NVP possible	No data
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.
RPV	PK Data	No data	<p>With DTG 50 mg Once Daily:</p> <ul style="list-style-type: none"> ↔ DTG AUC and C_{min} ↑ 22% ↔ RPV AUC and C_{min} ↑ 21% 	↑ or ↓ EVG, COBI, and RPV possible	<p>↔ RPV</p> <p>RAL C_{min} ↑ 27%</p>
	Dose	No dose adjustment needed.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.
PIs					
ATV	PK Data	<p>ATV 400 mg Once Daily plus BIC 75 mg Single Dose:</p> <ul style="list-style-type: none"> BIC AUC ↑ 315% 	<p>(ATV 400 mg plus DTG 30 mg) Once Daily:</p> <ul style="list-style-type: none"> DTG AUC ↑ 91% and C_{min} ↑ 180% 	↑ or ↓ EVG, COBI, and ATV possible	No data
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.
ATV/c	PK Data	BIC AUC ↑ 306%	No data	Not applicable	No data
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister two COBI-containing products.	No dose adjustment needed.

Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 4)

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
PIs, continued					
ATV/r	PK Data	↑ BIC expected	(ATV 300 mg plus RTV 100 mg) Once Daily plus DTG 30 mg Once Daily: • DTG AUC ↑ 62% and C _{min} ↑ 121%	Not applicable	With Unboosted ATV: • RAL AUC ↑ 72% With Unboosted ATV and RAL 1,200 mg: • RAL AUC ↑ 67% With (ATV 300 mg plus RTV 100 mg) Once Daily: • RAL AUC ↑ 41%
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.
DRV	PK Data	Not applicable	Not applicable	↔ DRV or EVG expected	Not applicable
	Dose	Do not administer DRV without RTV or COBI.	Do not administer DRV without RTV or COBI.	No dose adjustment needed.	Do not administer DRV without RTV or COBI.
DRV/c	PK Data	BIC AUC ↑ 74%	DRV/c plus DTG Once Daily: • ↔ DTG, DRV, and COBI DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c: • DTG C _{min} ↑ 100%	Not applicable	No data
	Dose	No dose adjustment needed.	No dose adjustment needed.	Do not coadminister two COBI-containing products.	No dose adjustment needed.
DRV/r	PK Data	No data	(DRV 600 mg plus RTV 100 mg) Twice Daily with DTG 30 mg Once Daily: • DTG AUC ↓ 22% and C _{min} ↓ 38%	Not applicable	With (DRV 600 mg plus RTV 100 mg) Twice Daily: • RAL AUC ↓ 29% and C _{min} ↑ 38%
	Dose	No dose adjustment needed.	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.
LPV/r	PK Data	No data	With (LPV 400 mg plus RTV 100 mg) Twice Daily and DTG 30 mg Once Daily: • ↔ DTG	Not applicable	↓ RAL ↔ LPV/r
	Dose	Consider alternative combination.	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.
TPV/r	PK Data	↓ BIC possible	With (TPV 500 mg plus RTV 200 mg) Twice Daily and DTG 50 mg Once Daily: • DTG AUC ↓ 59% and C _{min} ↓ 76%	Not applicable	With (TPV 500 mg plus RTV 200 mg) Twice Daily and RAL 400 mg Twice Daily: • RAL AUC ↓ 24% and C _{min} ↓ 55%

Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 4 of 4)

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
PIs, continued					
TPV/r	Dose	Do not coadminister.	In Patients Without INSTI Resistance: <ul style="list-style-type: none"> DTG 50 mg twice daily In Patients With Certain INSTI-Associated Resistance^a or Clinically Suspected INSTI Resistance: <ul style="list-style-type: none"> Consider alternative combination. 	Do not coadminister RTV and COBI.	RAL 400 mg twice daily Coadministration with RAL 1,200 mg once daily is not recommended.

^a Refer to DTG product label for details.

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{min} = minimum plasma concentration; COBI = cobicistat; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TPV = tipranavir; TPV/r = tipranavir/ritonavir